EXHIBIT D

Interference No. 104,761
University of New Mexico v. Fordham University

Filed on behalf of Party FORDHAM UNIVERSITY Paper _____

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES
(Administrative Patent Judge Torczon)

UNIVERSITY OF NEW MEXICO
(5,747,332 and 6,066,716),

Junior Party,

v.

FORDHAM UNIVERSITY
(09/090,754),

Senior Party.

Patent Interference No. 104,761

FORDHAM MISCELLANEOUS MOTION 4 UNDER 37 C.F.R. § 1.635
(Request for APJ to Exercise His Discretion under Rule 642)

Interference No. 104,761
University of New Mexico v. Fordham University

FORDHAM MISCELLANEOUS MOTION 4 UNDER 37 C.F.R. § 1.635
(Request for APJ to Exercise His Discretion under Rule 642)

I. STATEMENT OF PRECISE RELIEF REQUESTED

Fordham hereby moves pursuant to 37 C.F.R. § 1.635 to have the Administrative Patent Judge exercise his discretion under 37 C.F.R. § 1.642 and declare an additional interference between Fordham Application Serial No. 09/090,754 ("the '754 application") involved in interference 104,761 and UNM's U.S. Patent 6,433,141 ("the '141 patent").

The interfering claims include patentable claims 68, 69, 71-75, and 82-88 of Fordham's '754 application, designated as corresponding to Count 3, and claims 1-18 of the '141 patent.

More specifically, Fordham's present motion under 37 CFR § 1.635 requests that the APJ exercise his discretion under 37 CFR § 1.642 either to designate claims 1-18 the '141 patent to correspond to Count 3 of the present interference or, in the alternative, to add Fordham proposed claims 97-110 to Fordham's involved '754 application and define Fordham proposed claim 97 as new Count 5 and designate claims 1-18 of the '141 patent and Fordham's proposed claims 97-110 as corresponding thereto.

The present motion is being filed pursuant to the ORDER of Paper 95 of Patent Interference 104761. The present motion is being filed at this time and in this manner in order to obviate needless delay and expense pursuant to the Order of Paper 95.

II. EVIDENCE RELIED UPON

1. U.S. Patent No. 6,433,141 (Fordham Exhibit 1040)

2. Li (1993) *EMBO J.* 12(8): 3143-51 (Fordham Exhibit 1017).

3. Blachere (1993) *J. Immunotherapy* 14: 352-356 (Fordham Exhibit 1018).

4. Udono (1993) *J. Exp. Med.* 178: 1391-1396. (Fordham Exhibit 1019)

5. Udono (1994) *J. Immunol.* 152: 5398-5403. (Fordham Exhibit 1020).

6. Amino Acid Sequence Comparison gp96 and grp94 (Fordham Exhibit 1041)

7. Preliminary Amendment (Fordham Exhibit 1011) filed January 13, 1999, in connection with Fordham's involved '754 application.

8. Fordham Application Serial No. 09/090,754 (Fordham Exhibit 1035).

9. Nieland (1996) *Proc. Natl. Acad. Sci.* 93: 6135-6139. (Fordham Exhibit 1042)

10. Table Comparing Patentable Claims of Fordham's '754 application with claims 1-18 of the '141 patent, which define the same invention (Fordham Exhibit 1043).

11. Office Action mailed May 28, 1998, in connection with UNM's '139 application (which issued as UNM's involved '716 patent) (Fordham Exhibit 1044).

12. Office Action mailed September 23, 1999 in connection the '139 application (Fordham Exhibit 1045; page 2 of this Office Action is missing in the copy provided by the PTO)

13. Amendment filed by UNM on December 22, 1999 (Fordham Exhibit 1046), in connection with the '139 application (which issued as UNM's involved '716 patent).

14. Preliminary Amendment (Fordham Exhibit 1047) filed June 23, 2000, by UNM , in connection with UNM's '381 application (which issued as the '141 patent).

15. Office Action mailed May 22, 2001 (Fordham Exhibit 1048), in connection with the '381 application (which issued as the '141 patent).

16. Final Office Action mailed November 6, 2001 (Fordham Exhibit 1049), in connection with the '381 application (which issued as the '141 patent)

17. UNM Request for Reconsideration filed February 6, 2002, (Fordham Exhibit 1050), in connection the '381 application (which issued as the '141 patent).

18. Csermely (1991) *J. Biol. Chem.* 266(8): 4943-50. (Fordham Exhibit 1023).

19. Fordham's involved application Serial No. 09/090,754 (Fordham Exhibit 1035).

20. Lindquist (1988) *Ann. Rev. Genet.* 22: 631-677. (Fordham Exhibit 1027).

21. Gething (1992) *Nature* 355: 33-45 (Fordham Exhibit 1028).

22. Office Action mailed May 12, 1999, in connection with UNM's '139 application (which issued as UNM's involved '716 patent) (Fordham Exhibit 1051).

III. STATEMENT OF FACTS

1. A copy of the Notice Declaring Interference for Interference 104,761 was mailed to counsel for UNM, on October 12, 2001. This Notice included a copy of Fordham's claims, now designated as corresponding to Count 3, that recite ternary hsp-ADP-peptide complexes.

2. On October 26, 2001, in connection with the present interference Counsel for UNM filed a request for File Copies of Fordham's involved '754 and parent '391applications.

3. The file history of Fordham's involved '754 application included the Preliminary Amendment filed January 13, 1999 (Fordham Exhibit 1011) that amended the specification to disclose, explicitly, that the method of synthesis of heat shock protein complexes described at

page 36, *ll.* 25-32, inherently produced ternary complexes, *e.g.* hsp70-ADP-peptide complexes (Evidence ¶ 7, p. 12, 2nd full paragraph; p. 4 ll. 18-19).

4. Fordham's involved '754 application discloses that heat shock proteins belonging to the hsp90 family, including hsp90, gp96, and grp94, can be used in the invention of the '754 application (Evidence ¶ 19 p. 15, ll. 29-31, p. 16, ll. 8-24, and at p. 16, l. 25, in the table, previously incorporated by reference, that was inserted into the specification in the Preliminary Amendment (Evidence ¶ 7, p. 12, 2nd full paragraph; p. 3, "Table 1")).

5. The terms Gp96 and Grp94 refer to the same protein. (Evidence ¶ 9, p. 6135, left column, first sentence: "gp96, also known as GRP94, is a member of the HSP90 family..."; Evidence (Li) ¶ 2, p. 3143, first sentence of first full paragraph: "Comparison of the gp96 sequence to known sequences revealed significant homology with the heat shock protein (HSP) hsp90 and possible identity with the glucose-related protein grp94." (Citations omitted).

6. An amino acid sequence comparison between gp96 (Genbank sequence accession number gi: 18579009; 719 amino acids) and a precursor of grp94 (Genbank sequence accession number gi: 119360; 803 amino acids) revealed that amino acid residues 1-719 of gp96 are identical to amino acid residues 85 to 803 of grp94 (Evidence ¶ 6).

7. An amino acid sequence comparison between gp96 (Genbank sequence accession number gi: 18579009; 719 amino acids) and hsp90 (Genbank sequence accession number gi: 32488; 732 amino acids) revealed that 46% of the residues were identical (336/715), and 64% of the amino acid residues were positive (468/715). Hsp90 has been stated to be the "cytosolic counterpart of gp96." (Evidence ¶ 4, p. 1391, left col. 1st par., last sentence).

8. In the Office Action mailed May 28, 1998, in connection with the '139 application, which issued as UNM's '716 patent, pending claims 24-36 were rejected over claims 1-23 of UNM's involved '332 patent under the judicially created doctrine of double patenting (Evidence ¶ 11, p. 3, paragraph 3). The Examiner stated that "there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application [including therefore, claims 28 and 30-34; *see* Fact ¶ 9, below] during prosecution of the application which mature into a patent." This rejection was obviated by UNM's filing of a terminal disclaimer.

9. In the Office Action mailed May 12, 1999, (Evidence ¶ 22, pp. 3-5) in connection with UNM's '139 application, claim 30 was rejected under 35 U.S.C. § 102(e) and claims 28 and 30 to 34 were rejected under 35 U.S.C. § 103(a), over U.S. Patent No. 5,837,251 (the parent of Fordham's involved '754 application). Pending claims 30-34 correspond, essentially, to claims 2-6, 8-12, and 14-18 of the '141 patent. Pending claim 28 recited the following:

> Claim 28: A purified ADP-heat shock protein-peptide complex, wherein said heat shock protein is selected from the group consisting of hsp90, gp96, and grp94.

10. In the Office Action mailed September 23, 1999, in connection with UNM's '139 application, the rejection of claim 30, under 35 U.S.C. § 102(e), and claims 28 and 30 to 34 under 35 U.S.C. § 103(a), over Fordham's '251 patent (the parent of Fordham's involved '754 application), were maintained (Evidence ¶ 12, p. 3), even though claim 28 had been amended to recite only complexes comprising grp94.

11. In response to the Office Action mailed September 23, 1999, in connection with UNM's '139 application, UNM canceled claims 28 and 30-34 without prejudice (Evidence ¶ 13).

12. On March 24, 2000, counsel for UNM filed the '381 application as a divisional of UNM's '139 application, and, by Preliminary Amendment filed March 24, 2000, filed new claims 24-41 which correspond to claims 1-18 of the'141 patent (after amendment of the independent claims to recite "A purified ADP-heat shock protein -peptide complex"). Therefore, the three independent claims in the '141 patent, 1, 7, and 13 correspond to independent claim 28 of UNM's '139 application (which recited a Markush group consisting of hsp90, gp96, and grp94) but were written as three independent claims, each reciting a single member of this Markush group. Independent claim 30 of UNM's '139 application was re-written as a dependent claim and used three times, as claims 2, 8, and 14, of the '141 patent. Dependent claims 31-34 of UNM's '139 application correspond to dependent claims 3-6, 10-13, and 15-18 of the '141 patent.

With respect to support in the specification for new claims 24-41, UNM only stated in the Preliminary Amendment that "the newly added claims 24 to 41 are based entirely on the originally filed specification" of Application Serial No. 08/717,239. (Evidence ¶ 14)

13. In a first Office Action mailed May 22, 2001, pending claims 24-41 of UNM's '381 application were rejected under 35 U.S.C. § 103(a) over Fordham's '251 patent in combination with two other references (Evidence ¶15).

14. In a Final Office Action mailed November 6, 2001, amended claims 24-41 of UNM's '381 application were again rejected under 35 U.S.C. § 103(a) over Fordham's '251 patent in combination with two other references (Evidence ¶ 16).

15. On February 4, 2002, Fordham filed Miscellaneous Motion 2, requesting that an interference be declared between Fordham's involved claims reciting hsp70-ADP-peptide complexes and the corresponding claims of UNM's '716 patent.

16. On February 7, 2002, Interference 104761 was re-declared to include claims of the '716 patent and claims of Fordham's involved '754 application (Paper 40).

17. On February 6, 2002, UNM filed a Request for Reconsideration in response to the Final Office Action mailed November 6, 2002, submitting the following arguments:

(a) "Srivastava '251 describes using different purification methods for hsp70, hsp90, and gp96 complexes due to the differences between these three types of complexes (See Srivastava '251, Col. 13, line 47 to Col. 17, line 3). Therefore, Srivastava '251 cannot teach or suggest the ADP-hsp90-peptide complex of claim 24." (Evidence ¶ 17 at p. 2, 1st par.; at p. 6, 1st par., with respect to gp96; and at p. 10, 1st par., with respect to grp94 complexes).

(b) Dr. Srivastava's Declaration of December 21, 1997, and the '251 patent contradict the Examiner's assertion regarding modification of the teachings the '251 patent to include complexes of hsp90 and gp96 because substituting hsp90, gp96 or grp94 in a purification process for hsp70 was not obvious. (Evidence ¶ 17 at p. last par.; at p. 6, last par., re: gp96 complexes; and at p. 9, last par., re: grp94 complexes).

(c) UNM also alleged that "neither the May 22, 2001 Office Action nor the November 6, 2001 Office Action has provided a reference [although the '251 patent was cited] that teaches or suggests a method for making the purified complex of claim 24." (Evidence ¶ 17 at p. 3, last sent. of the 1st full par; at p. 7, 1st full par., re: gp96 complexes; and at p. 11, 1st full par., re: grp94).

(d) UNM also alleged that the '251 patent did not "teach or suggest a method for forming a non-naturally occurring ADP-hsp90-peptide complex." (Evidence ¶ 17 at p. 4, last par., 1st sent.; at p. 8, last par., re: gp96 complexes and at p. 12, last par.; re: grp94 complexes).

(e) UNM also alleged that the "Examiner has provided no reference teaching or suggesting that hsp90 may be 'substituted' for hsp70 in any complex, much less in an ADP-hsp70-peptide complex." (Evidence ¶ 17 at p. 5, 2nd full par.; at p. 9, 2nd full par., re: gp96 complexes of claims 30-35; and at p. 13, 3rd full par., re: grp94 complexes of claims 36-41).

18. The '381 was allowed, without explanation by the Examiner, on March 21, 2002, and the '141 patent issued on August 13, 2002.

19. Heat shock protein gp96 forms a stable complex with ATP, with ADP, and with peptides. (Evidence ¶ 2 at: p. 3143, Abstract; p. 3144, left col., 1st full par., 1st sent.; p. 3144, left col., 3rd full par.; p. 3145 Fig. 3B; p. 3147, par. entitled "Gp96 is associated with peptides.").

20. Heat shock protein hsp90 binds ATP (Evidence ¶ 2, p. 3144, left col., 1st full par. and Fig. 2, right column), can be bound to and eluted from an ATP-column (Evidence ¶ 18, p. 4945, right col., Table 1), and has been reported to associate with a "diverse array" of proteins (Evidence ¶ 21, p. 41, left col., last par., lines 1-7), and to form stable complexes with peptides (Evidence ¶ 5, p. 5402, left col. last par.).

21. Hsp70 forms a stable complex with ATP, with ADP (Evidence ¶ 2, p. 3144, left col., third full par., and p. 3145, Fig. 3B), and with peptides (Evidence ¶ 4, p. 1391, abstract, and Fig. 4, p. 1395; Evidence ¶5, p. 5402, left col. last par.).

22. Hsp70, hsp90, and gp96 complexes isolated from tumor tissue can be used to vaccinate animals against implanted tumor cells of the same type as those from which the hsp complexes are isolated. This specific immunogenicity is believed to derive from the non-covalently-bound peptides rather than the hsp, *per se*. (Evidence ¶ 3, p. 352, Abstract).

23. The ATP binding-region of gp96 has been identified within a 25 amino acid sequence (amino acids 154 to 178 of GenBank Accession No. gi: 18579009) beginning with the amino acids GNTLGRGT and ending with the amino acids KEEASDYLELD, where the 7 underlined residues are highly conserved (Evidence ¶ 2, p. 3144, Fig. 1). The corresponding 25 amino acid sequence in hsp90 has 12 amino acids that are identical (48% identity) to those in gp96 as well as 5 amino acids that "positively" correspond to those in gp96 (*i.e.* conservative replacements, such as serine for threonine, or aspartic acid for glutamic acid) (for a total of 17 residues either identical or positive, *i.e.* 68%). Of the 7 highly conserved residues in the gp96 sequence above, 6 are identical in the hsp90 sequence (Evidence ¶ 6; comparison between gi: 18579009 (gp96) and gi: 32488 (hsp90)).

24. Almost all organisms produce heat shock proteins, which are among the most highly conserved proteins in nature. (Evidence ¶ 20 page 632, lines 1-9).

25. Protein Chaperones include members of the hsp70, and hsp90 families. These proteins have different roles in the cell but their biochemical function depends upon their ability to bind to other proteins. (Evidence ¶ 21 page 35, left column, last paragraph, lines 1-5; page 35, right column, first full paragraph, lines 1-3, and Tables 1 and 2 at pages 35 and 37, respectively).

IV. THE PATENT CLAIMING INTERFERING SUBJECT MATTER

The UNM patent to be brought into the present interference is U.S. Patent No. 6,433,141 ("the '141 patent"), which issued on August 13, 2002, from Application Serial No. 09/534,381, filed March 24, 2000.

V. SERVICE OF A COMPLETE COPY OF THE FILE HISTORY

A complete copy of the file history of Application Serial No. 09/534,381 was served by Federal Express on Paul Adams, Esq., lead attorney for the University of New Mexico, on September 27, 2002.

VI. SUBJECT MATTER CLAIMED IN THE INTERFERING CLAIMS

Claims 1, 7, and 13 of the '141 patent recite ternary hsp-ADP-peptide complexes wherein the heat shock protein is hsp90, grp96, and grp94, respectively. Claims 2, 8, and 14 of the '141 patent depend on Claims 1, 7, and 13, respectively, and recite an hsp-peptide combination that is "non-naturally occurring." Claims 3, 9, and 15 of the '141 patent depend on Claims 2, 8, and 14, respectively, and recite an hsp-peptide combination in which the hsp is isolated from one cell of an individual and the peptide is isolated from a second cell of the same individual. Claims 4, 10, and 16 of the '141 patent depend on Claims 2, 8, and 14, respectively, and recite an hsp-peptide combination in which the hsp and peptide are from different individuals. Claims 5, 11, and 16 of the '141 patent depend on Claims 2, 8, and 14, respectively, and recite an hsp-peptide combination in which the hsp and the peptide are from different organisms. Claims 6, 12, and 18 of the '141 patent depend on Claims 2, 8, and 14, respectively, and recite an hsp-peptide combination in which the hsp and the peptide are from different species.

VII. REASONS WHY RELIEF SHOULD BE GRANTED

A. Legal Requirements for Adding a Patent to An Ongoing Interference

Where a patent claims the same patentable invention as a count in an interference authorization for a Motion to add that patent to an ongoing interference is provided by 37 CFR § 1.642. Fordham submits that Claims 1-18 of the '141 patent, assigned to UNM, define the same patentable invention as claims 68, 69, 71-75, and 82-88 of Fordham's involved

'754 application. (*See* Fordham Exhibit 1043, Table Comparing Fordham's patentable claims with claims 1-18 of the '141 patent).

Accordingly, if claims 1-18 of the '141 patent were designated to correspond to Count 3, an interference-in-fact would exist with Fordham's claims that correspond to Count 3, since, under 37 CFR § 1.601(j) "[a]n interference-in-fact exists when at least one claim of a party that is designated as corresponding to a count and at least one claim of an opponent that is designated to correspond to the count define the same patentable invention." The phrase "same patentable invention" is defined by 37 CFR § 1.601(n).

Determination of whether an interference-in-fact exists relies upon a two-way patentability analysis in which each of the subject inventions is, in turn, deemed to be prior art to the other. If, in each instance, each invention would be anticipated by or be obvious over the other, where the other is deemed to be prior art, then an interference-in-fact between the inventions has been established. (*Winter v. Fujita*, 53 USPQ2d 1234, 1243 (BPAI 1999)).

An invention is obvious under 35 U.S.C. § 103(a), if the "differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art." Relevant factual inquiries underlying the legal conclusion of obviousness include an evaluation of the scope and content of the prior art, the level of skill in the art, and the differences between the prior art and the claimed invention. (*In re Dembiczak*, 50 USPQ2D 1614, 1616 (Fed. Cir. 1999)).

B. Background Information Regarding Heat Shock Proteins

Heat shock proteins include those polypeptides synthesized by an organism in response to heat, and/or other physiological stress. Production of hsp's under these circumstances represents "the most highly conserved genetic system known, existing in every organism in which it has been sought, from archaebacteria to eubacteria, from plants to animals. Although certain features of the response vary from organism to organism, many are universal, or nearly so. All organisms examined produce proteins encoded by the hsp70 and hsp90 gene families in response to elevated temperatures. These proteins are among the most highly conserved proteins in existence." (Fact ¶ 24).

Heat shock proteins have also been referred to as protein chaperones based upon their ability to bind to partially folded proteins and facilitate their correct folding. Chaperones are generally members of the hsp60, hsp70, and hsp90 family (Fact ¶ 25) and may perform many different roles in various cells and organelles. However, each of these functions appears to be variations on the ability of heat shock proteins to bind to peptide sequences and modulate *e.g.* protein folding (Fact ¶ 25).

Specific Traits and Properties of Individual Heat Shock Proteins That Are Conserved Across Family "Boundaries"

Although many heat shock protein species have been identified (Fact ¶ 25), they share two specific traits that are clearly highly conserved among heat shock proteins even when considered as a "superfamily" encompassing, *e.g.* the hsp70 and hsp90 protein families: (1) adenine ribonucleotide binding and (2) peptide binding. Therefore, at the time of the present invention, those skilled in the art appreciated that heat shock proteins possessed these two highly conserved properties, even though substantial differences existed among hsps with respect to their molecular weight, amino acid sequence, intracellular location and specific intracellular role.

Known Properties of Hsp90 Family Members gp96 and grp94

Before September 20, 1996, the filing date of the application to which the '141 patent claims priority, gp96 and grp94 were considered to be the same protein by those of ordinary skill in the art (Fact ¶¶ 5 and 6). Accordingly, Fordham submits that the following information applies to gp96 as well as to grp94, which may be referred to collectively as gp96/grp94.

It had been established in the prior art that gp96 possessed an ATP-binding site, and that gp96 bound ATP and formed stable binary complexes, both with peptides (gp96-peptide) and with ADP (gp96-ADP) (Fact ¶¶ 19 and 23). It was also known that gp96-peptide complexes could be useful for the prevention and treatment of cancer and infectious disease, apparently as a result of the presence of immunogenic peptides non-covalently bound to gp96 (Fact ¶ 22).

Known Properties of the Hsp90 Family Member hsp90

It was also known that hsp90 and gp96 were members of the same heat shock protein family, that hsp90 was considered the cytosolic counterpart of gp96 and that hsp90 and gp96 shared substantial amino acid sequence homology (46% identity and 64% similarity; Fact ¶ 7). Moreover, it was also known that hsp90 bound ATP and could be bound to and eluted from an ATP-column (Fact ¶ 20), and that the ATP-binding site of hsp90 apparently was closely related to that of gp96 (Fact ¶ 23). Hsp90 had also been reported to bind to peptides and to a "diverse array" of proteins (Fact ¶ 20). It was also known that hsp90-peptide complexes could be useful for the prevention and treatment of cancer and infectious disease, apparently as a result of the presence of immunogenic peptides non-covalently bound to hsp90 (Fact ¶ 22).

Known Properties of the Hsp70 Family Member hsp70

Similarly, it had been established in the prior art that hsp70 bound ATP, and formed stable binary complexes with peptides (hsp70-peptide) and with ADP (hsp70-ADP), and that hsp70-peptide complexes could be useful for the prevention and treatment of cancer and infectious disease, apparently as a result of the presence of immunogenic peptides non-covalently bound to hsp70 (Fact ¶¶ 19 and 22).

C. Each Invention Defined by Claims 1, 7, and 13 of the '141 Patent Is Obvious Over That Defined by Claims 68, 69, 82, and 83 of Fordham's '754 Application, In View of the Art

Oral Hearing on the Preliminary Motions Discussed the Same Issues As Raised in the Instant Motion

The present motion is directed, *inter alia*, toward the question as to whether ternary hsp-ADP-peptide complexes comprising a heat shock protein other than hsp70 are obvious over hsp70-ADP-peptide complexes. The same issue was raised concerning the separate patentability of methods for purification and synthesis of non-hsp70-containing hsp-complexes during the Oral Hearing on the Preliminary Motions held September 13, 2002, in connection with the present interference.

During that Hearing, the Board emphasized that the specification of the '332 patent only disclosed two examples directed toward purification of hsp70-complexes and did not provide any method for purification or synthesis of a non-hsp70-containing complex. Therefore, as the Board stated, UNM has relied solely on the mere listing of hsp species for enablement of claims of the '332 patent for purification and synthesis of complexes comprising an hsp other than hsp70. As stated during the Hearing, UNM has necessarily relied upon an implicit teaching that heat shock proteins are such highly conserved molecules having common biological activities that disclosure of a method relating to hsp70 make obvious the use of the same method for all hsp species listed.

In view of these observations by the Board, Fordham submits in the '141 patent, UNM

has claimed hsp90-ADP-peptide, gp96-ADP-peptide, and grp94-ADP-peptide complexes based solely on a disclosed method for purification of hsp70-complexes in combination with a statement indicating that hsp90, gp96, or grp94, are known members of the hsp90 family of heat shock proteins. That is, in view of hsp70-ADP-peptide complexes, UNM has only offered the additional statement that hsp90, gp96, and grp94 are known members of the hsp90 family to enable the hsp90-ADP-peptide, gp96-ADP-peptide, and grp94-ADP-peptide complexes claimed in the '141 patent. Accordingly, UNM has, in effect, necessarily asserted that ternary hsp90-ADP-peptide, gp96-ADP-peptide, and grp94-ADP-peptide complexes are each obvious over a ternary hsp70-ADP-peptide complex.

Differences Between Claims 1, 7, and 13 of the '141 Patent and the Prior Art

For the purposes of the first part of the two-way patentability analysis to establish the existence of an interference-in-fact, the prior art includes the information in the Section VII (B), above, as well as Fordham's involved claims 68, 69, 82, and 83. Fordham's involved claims disclose hsp-ADP-peptide ternary complexes and hsp-ADP-protein ternary complexes, wherein the heat shock protein is a member of the hsp70 family of proteins, which includes, *inter alia*, the protein species, hsp70. Accordingly, the only difference between independent claims 1, 7, and 13 of the '141 patent and the prior art, is that the hsp recited as part of the ternary hsp-ADP-peptide complexes of claims 1, 7, and 13, is hsp90, gp96, and grp94, respectively, rather than hsp70.

With respect to the question as to whether, in view of the above, it would have been obvious to one of ordinary skill in the art to substitute hsp90, gp96, and grp94 for hsp70 in the ternary hsp70-ADP-peptide complexes recited in Fordham's involved claims to arrive at the

invention defined by claims 1, 7, and 13, respectively, of the '141 patent, Fordham submits the following.

With respect to claim 7 of the '141 patent, Fordham submits that one of ordinary skill in the art would have been motivated to substitute gp96 for hsp70 in the ternary complex recited in Fordham claim 69, for example, with the expectation that such complexes could be useful for the prevention and treatment of cancer and infectious disease (Fact ¶ 22).

Moreover, one of ordinary skill would have had a reasonable expectation of success in forming ternary gp96-ADP-peptide complexes in view of the prior art's disclosure of hsp70-ADP-peptide complexes and in light of: (1) the adenine nucleotide binding and peptide sequence binding activities conserved among heat shock proteins; (2) the ability of gp96 (like hsp70) to form stable binary complexes with ADP; and (3) the ability of gp96 (like hsp70) to form stable binary complexes with peptides.

Therefore, each element of the invention of claim 7 of the '141 patent had been disclosed in the prior art. Moreover, the prior art also provided motivation to one of ordinary skill in the art to substitute gp96 for hsp70 in the ternary complex recited in Fordham claim 69, for example. Accordingly, Fordham submits that claim 7 of the '141 patent would have been obvious over Fordham claim 69, for example, which corresponds to Count 3. For the same reasons, Fordham further submits that claim 13 of the '141 patent would also have been obvious over Fordham claim 69, since the prior art indicated that gp96 and grp94 were, essentially, the same protein.

With respect to claim 1 of the '141 patent, Fordham submits that one of ordinary skill in the art would have been motivated to substitute hsp90 for hsp70 in the ternary complex recited in

Fordham claim 69, with the expectation that such complexes would be useful for the prevention and treatment of cancer and infectious disease (Fact ¶ 22).

Moreover, one of ordinary skill would have had a reasonable expectation of success in forming ternary hsp90-ADP-peptide complexes in view of the prior art's disclosure of hsp70-ADP-peptide complexes and in light of: (1) the adenine nucleotide binding and peptide sequence binding activities conserved among heat shock proteins; (2) the ability of hsp90 to form a stable complex with ATP; (3) the amino acid sequence homology shared between hsp90 and gp96 within the adenine ribonucleotide binding site of gp96, a protein known to form a stable binary complex with ADP (like hsp70); and (4) the ability of hsp90 (like hsp70) to form stable binary complexes with peptides. Therefore, each element of the invention defined by claim 1 of the '141 patent had been disclosed in the prior art. Moreover, the prior art also provided motivation to one of ordinary skill in the art to substitute hsp90 for hsp70 in the ternary complex recited in Fordham claim 69, for example. Consequently, Fordham submits that claim 1 of the '141 patent would have been obvious over Fordham claim 69, for example, which corresponds to Count 3.

Accordingly, each invention defined by independent claims 1, 7, and 13 of the '141 patent is the same patentable invention, as defined by 37 CFR § 1.601(n), as that of Fordham's involved claims 68, 69, 82, and 83, which correspond to Count 3.

D. Each Invention Defined by Claims 68, 69, 82, and 83 of Fordham's Involved '754 Application Would Be Obvious Over That Defined by Claims 1, 7, and 13 of the '141 Patent If the '141 Patent Were Prior Art to Fordham's Involved '754 Application

Differences Between Claims 68, 69, 82, and 83 of Fordham's Involved '754 Appliction and the Prior Art

For the purposes of this second part of the two-way patentability analysis to establish the existence of an interference-in-fact, the prior art is deemed to include includes the information in the Section VII (B) above as well as claims 1, 7, and 13 of the '141 patent, which recite hsp90-ADP-peptide, gp96-ADP-peptide, and grp94-ADP-peptide ternary complexes, respectively. Accordingly, the only difference between Fordham claims 68, 69, 82, and 83 of Fordham's involved '754 application and the "prior art," is that the hsp recited as part of the ternary hsp-ADP-peptide complexes of claims 68, 69, 82, and 83 of Fordham's involved '754 application, is a member of the hsp70 family, *e.g.*, the protein species, hsp70. [1]

The issue therefore, is whether it would have been obvious to one of ordinary skill in the art to substitute hsp70 in the ternary hsp90-ADP-peptide, gp96-ADP-peptide, and grp94-ADP-peptide complexes recited in claims 1, 7, and 13, respectively, of the '141 patent, to arrive at the invention defined by claims 68, 69, 82, and 83 of Fordham's involved '754 application.

Fordham submits that one of ordinary skill in the art would have been motivated to substitute hsp70 for hsp90, gp96, and grp94 in the ternary complex recited in claims 1, 7, and 13 of the '141 patent with the expectation that such complexes would be useful for the prevention and treatment of cancer and infectious disease (Fact ¶ 22).

Moreover, one of ordinary skill would have had a reasonable expectation of success in forming ternary hsp70-ADP-peptide and hsp70-ADP-protein complexes in view of the "prior art's" disclosure of hsp90-ADP-peptide, gp96-ADP-peptide, and grp94-ADP-peptide complexes

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[1] This is so, even though claims 82 and 83 of Fordham's involved '754 application recite hsp-ADP-protein complexes, since the word "peptides" has been defined in the '141 patent to encompass both peptides and polypeptides (Column 2, last sentence).

recited in claims 1, 7, and 13, respectively, of the '141, in light of: (1) the adenine nucleotide binding and peptide sequence binding activities conserved among heat shock proteins; (2) the ability of hsp70 to bind to ATP (like hsp90 and gp96/grp94); (3) the ability of hsp70 (like gp96/grp94) to form stable binary complexes with ADP; and (4) the ability of hsp70 (like hsp90 and gp96/grp94) to form stable binary complexes with peptides.

Therefore, each element of the invention was disclosed in the prior art. Moreover, the prior art also provided motivation to one of ordinary skill in the art to substitute hsp70 for hsp90, gp96, and grp94 in the ternary complex recited in claims 1, 7, and 13 of the '141 patent. Accordingly, Fordham submits that the invention defined by claims 68, 69, 82, and 83 of Fordham's involved '754 application would have been obvious over the invention defined in each of claims 7 and 13 of the '141 patent, if the '141 patent were prior art to Fordham's involved '754 application.

Therefore, each invention defined by Fordham's involved claims 68, 69, 82, and 83, which correspond to Count 3, would be the same patentable invention, as defined by 37 CFR § 1.601(n), as that of independent claims 1, 7, and 13 of the '141 patent, if the '141 patent were prior art to Fordham's involved '754 application.

In view of the conclusions reached in Sections VII(C) and VII(D), above, Fordham submits that an interference-in-fact exists between each invention defined by independent claims 1, 7, and 13 of the '141 patent, and claims 68, 69, 82, and 83 of Fordham's involved '754 application.

Fordham further submits that dependent claims 2, 8, and 14 of the '141 patent and Fordham's involved claims 71 and 82 would each be obvious over the other under the two-way

analysis carried out above for UNM's and Fordham's independent claims. UNM's dependent claims 2, 8, and 14 of the '141 patent do not recite any limitation that would result in a patentably distinct claim over Fordham's involved claims 71 and 82, since each of these claims recites an hsp-peptide combination that is not isolated from a natural source.

In addition, for the reasons provided in the preceding paragraphs and in view of the claim comparison set forth in Fordham Exhibit 1043, Fordham submits that: (1) dependent claims 3, 9, and 15 of the '141 patent and Fordham's involved claims 72 and 85 would each be obvious over the other, since each of these claims recites an hsp-peptide complex in which the hsp and peptide are from the same individual; (2) dependent claims 4, 10, and 16 of the '141 patent and Fordham's involved claims 73 and 86 would each be obvious over the other since each of these claims recites an hsp-peptide complex in which the hsp and peptide are from different individuals; (3) dependent claims 5, 11, and 17 of the '141 patent and Fordham's involved claims 74 and 87 would each be obvious over the other since each of these claims recites an hsp-peptide complex in which the hsp and peptide are from different organisms; and (4) dependent claims 6, 12, and 18 of the '141 patent and Fordham's involved claims 72 and 85 would each be obvious over the other since each of these claims recites an hsp-peptide complex in which the hsp and peptide are from different species.

VIII. The '141 PATENT INVOLVES INTERFERING SUBJECT MATTER EVEN IN VIEW OF THE PROSECUTION HISTORY OF APP. SER. NO. 09/534,381

Fordham submits that a very brief summary of the prosecution history of UNM's '139 and '381 applications would be helpful with respect to ascertaining why an additional interference was not declared and why the '141 patent issued without a terminal disclaimer.

During prosecution of UNM's '139 application (which issued as UNM's involved '716 patent), UNM claimed a ternary hsp-ADP-peptide complex as a composition of matter, wherein the hsp was selected from the group consisting of hsp90, gp96, and grp94. In addition, five claims of UNM's '139 application corresponded to claims 2-6, 8-12, and 14-18 of the '141 patent. However, these six claims were rejected under 35 USC § 103(a) over Fordham's '251 patent, the parent of Fordham's involved '754 application (Fact ¶ 9). This rejection was maintained (Fact ¶ 10), and, UNM then canceled these six claims without prejudice (Fact ¶ 11).

UNM subsequently filed the '381 application as a "division" of UNM's '139 application, adding 18 claims by Preliminary Amendment, that, with modification, issued as claims 1-18 in the '141 patent. UNM did not indicate where support for these new claims could be found in the specification as filed (Fact ¶ 12).

After an initial and final rejection of all pending claims in UNM's '381 application, UNM filed a request for reconsideration on February 6, 2002, that included five arguments (Fact ¶ 17, sections (a) - (e)).

UNM argued that Fordham's '251 patent disclosed different methods for purification of peptide complexes of hsp70, hsp90, and gp96 (Fact ¶ 17 (a)), and alleged that the '251 patent did not indicate that hsp90, gp96, and grp94 complexes could be purified according to the method disclosed for hsp70 complexes (Fact ¶ 17 (b)). UNM further argued that the Examiner had not provided any reference that taught or suggested a method for making hsp90-ADP-peptide, gp96-ADP-peptide, or grp94-ADP-peptide complexes, much less the non-naturally occurring complexes recited in claims 2, 8, and 14 of the '141 patent (Fact ¶ 17 (c) and (d)). UNM also alleged that the Examiner had not provided a reference that taught or suggested that hsp90, gp96,

and grp94 could be substituted for hsp70 in any complex, much less an hsp70-ADP-peptide complex (Fact ¶ 17 (e)).

Therefore, despite the fact that UNM's pending claims were directed toward ternary complexes as compositions of matter, and even though UNM was aware of Fordham's claims reciting hsp-ADP-peptide ternary complexes and Fordham's teaching regarding methods for formation thereof (Fact ¶¶ 1-4, and 15), UNM nevertheless argued that Fordham's '251 patent, did not teach or suggest a method of forming a ternary hsp-ADP-peptide complex where the hsp was hsp90, gp96, or gp94.

Fordham's review of the file history of UNM's '381 application suggests that the Examiner was not aware of the following information during prosecution of that application:

1. The method of formation of hsp complexes described at page 36, lines 25-32 of Fordham's parent '391 and involved '754 applications, inherently produced ternary hsp-ADP-peptide complexes and that the specification of both applications stated, at page 16, lines 6-24, that hsps belonging to the hsp90 family could be used in the practice of the invention disclosed. Moreover, hsp90 family members hsp90 and gp96 were explicitly recited in Fordham's parent '391 as filed, while description of the additional hsp90 species, grp94 was incorporated by reference.

2. Fordham had filed its involved '754 application, and by preliminary amendment, had amended the specification to explicitly recite and claim the inherent hsp-ADP-peptide ternary complexes formed, *e.g.*, according to the method described at page 36, lines 25-32 of Fordham's parent '391 and involved '754 applications.

3. That UNM's '716 patent, the immediate parent of UNM's '381 application, claiming ternary hsp-ADP-peptide complexes was involved in the present interference.

In addition, Fordham submits that art, such as *e.g.* Fordham Exhibits 1017-1020, that was particularly material (*see e.g.* § VII (B), above) to the patentability of claims 1-18 of UNM's '381 application Fordham was not cited against these claims during prosecution thereof, even though this art was of record.

Fordham submits that even though an interference-in-fact existed between UNM's '381 application and Fordham's involved '754 application, an interference was not declared apparently because the Examiner was unaware of the subject matter claimed in Fordham's involved '754 application.

Fordham notes that UNM's involved '716 patent issued with a terminal disclaimer, as required by the Examiner (Fact ¶ 8). However, the same Examiner elected not to impose the same requirement during prosecution of UNM's "divisional" '381 application, even though the factual basis for doing so did not appear to differ from that of UNM's '139 application. Fordham has no explanation for this apparently inconsistent action by the Examiner.

IX. Fordham Proposed Claims 97-110

Fordham submits that claims 1-18 of the '141 patent define the same patentable invention as that defined by Fordham's involved claims 68, 69, 71-75, and 82-88 and, therefore, on that basis, claims 1-18 of the '141 patent should be designated as corresponding to Count 3. However, should the APJ not agree with this conclusion, Fordham proposes, in the alternative, new claims 97-110 be added to Fordham's involved '754, that new Count 5, defined as Fordham

proposed claim 97, be added to the present interference, and that claims 1-18 of the '141 patent and Fordham claims 97-110 be designated as corresponding to proposed Count 5.

Therefore, if necessary and if authorized, Fordham would add claims 97-110, listed in Appendix 1, attached hereto, to Fordham's involved '754 application. Support for each of the limitations recited in claims 97-110 is found in Appendix 2, attached hereto. Fordham proposed Claims 97-103 recite hsp-ADP-peptide complexes while Fordham proposed claims 94-110 recite hsp-ADP-protein complexes (*see* Footnote 1, above).

Fordham submits that there is support for each of proposed claims 97-110 in Fordham's '391 application and Fordham's involved '754 application, which claims the benefit of the filing date of the '391 application.

X. ALTERNATIVE REMEDIES

As an alternative to declaring an additional interference at this time, Fordham could file a continuation application including Fordham's proposed claims 97-110, and a request could be made to the new Examiner to provoke an additional interference. However, Fordham submits that this would result in needless dely and expense for both Fordham and the University of New Mexico. No attempts have been made by Fordham, the Examiner for Fordham's involved '754 application, or, apparently the Examiner for UNM's '381 application, to provoke an additional interference.

XI. Conclusion

For the reasons provided above, an additional interference should be declared, pursuant to the discretion of the APJ under 37 C.F.R. § 1.642, between Fordham's involved '754 Application and the '141 patent. The claims involved would include Fordham's claims 68, 69, 71-75, and

82-88 and claims 1-18 of the '141 patent, which should be designated as corresponding to Count 3 of the present interference. Alternatively, Fordham's proposed claims 97-110 should be added to Fordham's involved '754 application, and a new count added, Count 5, which would be Fordham Claim 97, and Fordham's proposed claims 97-110 and claims 1-18 of the '141 patent designated as corresponding to new Count 5.

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30,605

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Appendix 1

Fordham's proposed claims to be added to the '754 application.

97. An ADP-heat shock protein 90-peptide complex in substantially purified form as indicated by apparent homogeneity upon electrophoresis in a polyacrylamide gel.

98. The ADP-heat shock protein 90-peptide complex of Claim 97, wherein said heat shock protein 90 comprises one of the group consisting of hsp90, gp96 and grp94.

99. The ADP-heat shock protein 90-peptide complex of Claim 97, wherein said ADP-heat shock protein 90-peptide complex comprises a heat shock protein90-peptide complex made *in vitro*.

100. The ADP-heat shock protein 90-peptide complex of Claim 99, wherein said heat shock protein 90-peptide complex comprises a heat shock protein 90 and a peptide from the same individual.

101. The ADP-heat shock protein 90-peptide complex of Claim 99, wherein said heat shock protein 90-peptide complex comprises a heat shock protein 90 from a first individual and a peptide from a second, different individual.

102. The ADP-heat shock protein 90-peptide complex of Claim 99, wherein said heat shock protein 90-peptide complex comprises a heat shock protein 90 from a first organism and a peptide from a second, different organism.

103. The ADP-heat shock protein 90-peptide complex of Claim 99, wherein said heat shock protein 90-peptide complex comprises a heat shock protein 90 from a first species and a peptide from a second, different species.

104. An ADP-heat shock protein 90-protein complex in substantially purified form as indicated by apparent homogeneity upon electrophoresis in a polyacrylamide gel.

105. The ADP-heat shock protein 90-protein complex of Claim 104, wherein said heat shock protein 90 comprises one of the group consisting of hsp90, gp96 and grp94.

106. The ADP-heat shock protein 90-protein complex of Claim 104, wherein said ADP-heat shock protein 90-protein complex comprises a heat shock protein90-protein complex made *in vitro*.

107. The ADP-heat shock protein 90-protein complex of Claim 106, wherein said heat shock protein 90-protein complex comprises a heat shock protein 90 and a protein from the same individual.

108. The ADP-heat shock protein 90-peptide complex of Claim 106, wherein said heat shock protein 90-protein complex comprises a heat shock protein 90 from a first individual and a protein from a second, different individual.

109. The ADP-heat shock protein 90-protein complex of Claim 106, wherein said heat shock protein 90-protein complex comprises a heat shock protein 90 from a first organism and a protein from a second, different organism.

110. The ADP-heat shock protein 90-peptide complex of Claim 106, wherein said heat shock protein 90-protein complex comprises a heat shock protein 90 from a first species and a protein from a second, different species.

Appendix 2

Support for Fordham Proposed claims 97-110 is found in the specification of Fordham's involved '754 application (Fordham Exhibit 1035) as indicated below:

97. An ADP-heat shock protein 90-peptide complex {**page 16 *ll.* 5-24; page 36 *ll.* 25-32, including text inserted by Preliminary Amendment on January 13, 1999 (Fordham Exhibit 1011)**} in substantially purified form {**page 23 *ll.* 8-18; page 25 *l.* 20 to page 29 *l.* 14; page 36 *ll.* 5-11; page 36 *ll.* 18-21; page 37 *ll.* 2-5**} as indicated by apparent homogeneity upon electrophoresis in a polyacrylamide gel {**page 30, *ll.* 20-25**}.

98. The ADP-heat shock protein 90-peptide complex of Claim 97, wherein said heat shock protein 90 comprises one of the group consisting of hsp90 {**page 15, lines 29-31 and page 16 *ll.* 5-24**}, gp96 {**page 15, lines 29-31 and page 16 *ll.* 5-24**} and grp94{**page 16 *ll.* 5-24, including the text and Table inserted by Preliminary Amendment on January 13, 1999 (Fordham Exhibit 1011)** }.

99. The ADP-heat shock protein 90-peptide complex of Claim 97, wherein said ADP-heat shock protein 90-peptide complex comprises a heat shock protein90-peptide complex made *in vitro* {**page 23, *ll.* 5-15 and page 35 *l.* 24 to page 37 *l.* 12**}.

100. The ADP-heat shock protein 90-peptide complex of Claim 99, wherein said heat shock protein 90-peptide complex comprises a heat shock protein 90 and a peptide from the same individual {**page 10 *ll.* 7-11**}.

101. The ADP-heat shock protein 90-peptide complex of Claim 99, wherein said heat shock protein 90-peptide complex comprises a heat shock protein 90 from a first individual and a peptide from a second, different individual {**page 10 *ll.* 7-11**}.

102. The ADP-heat shock protein 90-peptide complex of Claim 99, wherein said heat shock protein 90-peptide complex comprises a heat shock protein 90 from a first organism and a peptide from a second, different organism **{page 23 *ll.* 8-18, page 33 *ll.* 5-9, page 34 *l.* 28 to page 35 *l.* 22}**.

103. The ADP-heat shock protein 90-peptide complex of Claim 99, wherein said heat shock protein 90-peptide complex comprises a heat shock protein 90 from a first species and a peptide from a second, different species **{page 23 *ll.* 8-18, page 33 *ll.* 5-9, page 34 *l.* 28 to page 35 *l.* 22}**.

104. An ADP-heat shock protein 90-protein complex **{page 16 *ll.* 5-24; page 36 *ll.* 25-32, including text inserted by Preliminary Amendment on January 13, 1999 (Fordham Exhibit 1011), page 10 *ll.* 16-22, page 22 *l.* 30 to page 23 *l.* 4, page 32 *l.* 8, and page 36 *l.* 27}** in substantially purified form **{page 23 *ll.* 8-18; page 25 *l.* 20 to page 29 *l.* 14; page 36 *ll.* 5-11; page 36 *ll.* 18-21; page 37 *ll.* 2-5}** as indicated by apparent homogeneity upon electrophoresis in a polyacrylamide gel **{page 30, *ll.* 20-25}**.

105. The ADP-heat shock protein 90-protein complex of Claim 104, wherein said heat shock protein 90 comprises one of the group consisting of hsp90 **{page 15, lines 29-31 and page 16 *ll.* 5-24}**, gp96 **{page 15, lines 29-31 and page 16 *ll.* 5-24}** and grp94**{page 16 *ll.* 5-24, including the text and Table inserted by Preliminary Amendment on January 13, 1999 (Fordham Exhibit 1011) }**.

106. The ADP-heat shock protein 90-protein complex of Claim 104, wherein said ADP-heat shock protein 90-protein complex comprises a heat shock protein90-protein complex made *in vitro* **{page 23, *ll.* 5-15 and page 35 *l.* 24 to page 37 *l.* 12}**.

107. The ADP-heat shock protein 90-protein complex of Claim 106, wherein said heat shock protein 90-protein complex comprises a heat shock protein 90 and a protein {**page 10 *ll.* 16-22, page 22 *l.* 30 to page 23 *l.* 4, page 32 *l.* 8, and page 36 *l.* 27**} from the same individual {**page 10 *ll.* 7-11**}.

108. The ADP-heat shock protein 90-protein complex of Claim 106, wherein said heat shock protein 90-protein complex comprises a heat shock protein 90 from a first individual and a protein {**page 10 *ll.* 16-22, page 22 *l.* 30 to page 23 *l.* 4, page 32 *l.* 8, and page 36 *l.* 27**} from a second, different individual {**page 10 *ll.* 7-11**}.

109. The ADP-heat shock protein 90-protein complex of Claim 106, wherein said heat shock protein 90-peptide complex comprises a heat shock protein 90 from a first organism and a protein {**page 10 *ll.* 16-22, page 22 *l.* 30 to page 23 *l.* 4, page 32 *l.* 8, and page 36 *l.* 27**} from a second, different organism {**page 23 *ll.* 8-18, page 33 *ll.* 5-9, page 34 *l.* 28 to page 35 *l.* 22**}.

110. The ADP-heat shock protein 90-protein complex of Claim 106, wherein said heat shock protein 90-protein complex comprises a heat shock protein 90 from a first species and a protein {**page 10 *ll.* 16-22, page 22 *l.* 30 to page 23 *l.* 4, page 32 *l.* 8, and page 36 *l.* 27**} from a second, different species {**page 23 *ll.* 8-18, page 33 *ll.* 5-9, page 34 *l.* 28 to page 35 *l.* 22**}.